AL/CF-TR-1993-0073

CHRONIC PHYSIOLOGICAL EFFECTS OF POSITIVE PRESSURE BREATHING IN A HIGH SUSTAINED G ENVIRONMENT

Lloyd D. Tripp, Jr.
Steve Bolia

SYSTEMS RESEARCH LABORATORIES, INC.
2800 INDIAN RIPPLE ROAD
DAYTON OH 45440-3696

James Cooper

OCCUPATIONAL AND ENVIRONMENTAL HEALTH DIRECTORATE
VETERINARY SCIENCES DIVISION
WRIGHT-PATTERSON AFB OH 45433-7902

William B. Albery

CREW SYSTEMS DIRECTORATE
BIODYNAMICS AND BIOCOMMUNICATIONS DIVISION
WRIGHT-PATTERSON AFB OH 45433-7008

Gary B. Marit

ARMY MEDICAL RESEARCH UNIT
TOXICOLOGY DIVISION
WRIGHT-PATTERSON AFB OH 45433-7400

JANUARY 1993

FINAL REPORT FOR THE PERIOD DECEMBER 1991 - JUNE 1992

AIR FORCE MATERIEL COMMAND
WRIGHT-PATTERSON AIR FORCE BASE, OHIO 45433

NOTICE

When US Government drawings, specifications, or other data are used for any purpose other than a definitely related Government procurement operation, the Government thereby incurs no responsibility nor any obligation whatsoever, and the fact that the Government may have formulated, furnished, or in any way supplied the said drawings, specifications, or other data, is not to be regarded by implication or otherwise, as in any manner, licensing the holder or any other person or corporation, or conveying any rights or permission to manufacture, use or sell any patented invention that may in any way be related thereto.

Please do not request copies of this report from the Armstrong Laboratory. Additional copies may be purchased from:

National Technical Information Service
5285 Port Royal Road
Springfield VA 22161

Federal Government agencies and their contractors registered with Defense Technical Information Center should direct requests for copies of this report to:

Defense Technical Information Center
Cameron Station
Alexandria VA 22314

TECHNICAL REVIEW AND APPROVAL

AL/CF-TR-1993-0073

The experiments reported herein were conducted according to the "Guide for the Care and Use of Laboratory Animals, " Institute of Laboratory Animal Resources, National Research Council.

This report has been reviewed by the Office of Public Affairs (PA) and is releasable to the National Technical Information Service (NTIS). At NTIS, it will be available to the general public, including foreign nations.

This technical report has been reviewed and is approved for publication.

FOR THE COMMANDER

THOMAS J. MOORE, Chief
Biodynamics and Biocommunications Division
Crew Systems Directorate
Armstrong Laboratory

REPORT DOCUMENTATION PAGE

Form Approved
OMB No. 0704-0188

1. AGENCY USE ONLY *(Leave blank)*	2. REPORT DATE	3. REPORT TYPE AND DATES COVERED
	January 1993	Final Report for period December 1991 to June 1992

4. TITLE AND SUBTITLE

Chronic Physiological Effects Of Positive Pressure Breathing In A High Sustained G Environment

5. FUNDING NUMBERS

C - F33615890C0574
PE - 61101F
PR - ILIR
TA - ILIRBB
WU - ILIRBB10

6. AUTHOR(S)

Lloyd D. Tripp Jr., Steve Bolia, James Cooper
William B. Albery, Gary B. Marit

7. PERFORMING ORGANIZATION NAME(S) AND ADDRESS(ES)

Systems Research Laboratories Inc.
2800 Indian Ripple Road
Dayton OH 45440-3696

8. PERFORMING ORGANIZATION REPORT NUMBER

9. SPONSORING/MONITORING AGENCY NAME(S) AND ADDRESS(ES)

Armstrong Laboratory, Crew Systems Directorate
Biodynamics and Biocommunications Division
Human Systems Center
Air Force Materiel Command
Wright-Patterson AFB OH 45433-7008

10. SPONSORING/MONITORING AGENCY REPORT NUMBER

AL/CF-TR-1993-0073

11. SUPPLEMENTARY NOTES

12a. DISTRIBUTION/AVAILABILITY STATEMENT

Approved for public release; distribution is unlimited

12b. DISTRIBUTION CODE

13. ABSTRACT *(Maximum 200 words)*

A new Positive Pressure Breathing system for G protection (PBG) known as COMBAT EDGE, is currently being evaluated for both USAF and NAVY F-16 and F-15 aircraft. This system is being used in conjunction with the current Air Force standard CSU-13B/P anti-G suit. Once this system is fully deployed, pilots can be exposed to a high time duration dose of positive pressure breathing over the course of a 20 year flying career. Recent concerns in this area have been raised by the Aerospace Medical Community as to the possibility of occupational hazards associated with long duration exposure to PPB. This study addresses those questions by studying both the physiological and histopathological effects of long duration exposure to PPB. In this study, four, protected Minihanford miniature swine were exposed over 27 days to 10 minute exposures of continuous high sustained acceleration on a 20.5 ft. radius centrifuge. Two-dimensional echocardiograms were accomplished prior to G exposure and again after the exposure at day 27. In addition, aortic pulmonary pressure, respiration, heart rate, and cardiac output data were collected on experimental test day 1 and 27. Necropsy and subsequent histopathological examinations of major organs were accomplished. This study found no significant pathophysiological changes which could be attributed to the chronic exposure to PPB.

14. SUBJECT TERMS	15. NUMBER OF PAGES
Minihanford Miniature Swine, Positive Pressure Breathing, Respiration, Simulated Aerial Combat Maneuver, Anti-G Suit, high Sustained G, Arterial Pressure, Pulmonary Pressure	39
	16. PRICE CODE

17. SECURITY CLASSIFICATION OF REPORT	18. SECURITY CLASSIFICATION OF THIS PAGE	19. SECURITY CLASSIFICATION OF ABSTRACT	20. LIMITATION OF ABSTRACT
UNCLASSIFIED	UNCLASSIFIED	UNCLASSIFIED	UNLIMITED

THIS PAGE LEFT BLANK INTENTIONALLY

Preface

Research was performed under WU ILIRBB10 as a FY 90 Innovative Independent Laboratory Research program. Drs. James Cooper and William Albery were co-principal investigators. The research was conducted through the Engineering Services Contract number F-33615-89-C-0574 by Systems Research Laboratories. The authors wish to thank Susan Young from the Armstrong Laboratory Vivarium, Mr. Alva Karl, Melissa Frey, and Beverly Girten from Systems Research Laboratories; Lt.Col John Latendresse from the Army Medical Research Unit, Toxicology Division; Mr. Chuck Goodyear and Deepa Naishadham from Logicon Technical Services Inc who provided statistical analysis support, and a special thanks to Miss Grady Ripley of Krug International who tailored the G suits used in this study; Bill Collins of the Research Enginering and Fabrication Office, Brooks AFB, TX who hand molded the PPB snout mask; Dr. John Burns of the School of Armstrong Laboratory, Brooks AFB, TX; Dr. John Bonigura from the Ohio State University School of Veterinarian Medicine, who performed and analyzed the two-dimensional echocardiograms; the Dynamic Environment Simulator operation crew; and Mrs. Tamara Chelette of the Combined Stress Branch, Armstrong Laboratory who helped in organizing this study.

The animals used in this study were handled in accordance with the principles stated in the Guide for the Care and Use of Laboratory Animals, prepared by the Committee on Care and Use of Laboratory Animals of the Institute of Laboratory Animal Resources, National Research Council, DHHS, National Institute of Health Publication #85-23, 1985, and the Animal Welfare Act of 1966, as amended.

ABBREVIATIONS USED

LA-2D - Left atrial dimension using two-dimensional imaging

Aorta - aortic dimension

RR - ECG R wave to R wave time interval

LVWd - Left ventricular wall dimension

LVIDd - Left ventricular interior diameter at end-diastole

IVSd - Interventricular septum dimension

RVIDd - Right ventricular interior diameter at diastole

LVWs - Left ventricular wall dimension at end-systole

LVIDs - Left ventricular interior diameter at end-systole

IVSs - interventricular septum dimension at end-systole

IVSamp - Excursion of the ventricular septum in systole

IVScv - Intraventricular septum curvature

RVWd - Right ventricular wall dimension

RA2D - Right atrium two dimensional echocardiogram

PA - Pulmonary artery dimension

PA_vel - Pulmonary artery velocity

TV_E_vel - Tricuspid valve end-flow velocity

TV_A_vel - Tricuspid valve arterial contraction velocity

Pl_vel - Pulmonary insufficiency velocity

RA/LA - Right atrium/left atrium ratio

RVw/LVw - Right ventricular wall/Left ventricular wall ratio

RVid/LVid - Right ventricular interior/Left ventricular interior dimension ratio

PA/AO - Pulmonary artery dimension/Aortic dimension ratio

LV_SF % - Left ventricular shortening fraction % change from baseline

ATAGS - Advanced technology anti-G suit

PPB - Positive Pressure Breathing

mm Hg - Millimeters of mercury

B.W. - Body weight

Vent - Ventricle

kg - Kilogram

gm - Gram

mg - Milligram

Hz - Hertz

psi - Pounds per square inch

TABLE OF CONTENTS

LIST OF FIGURES

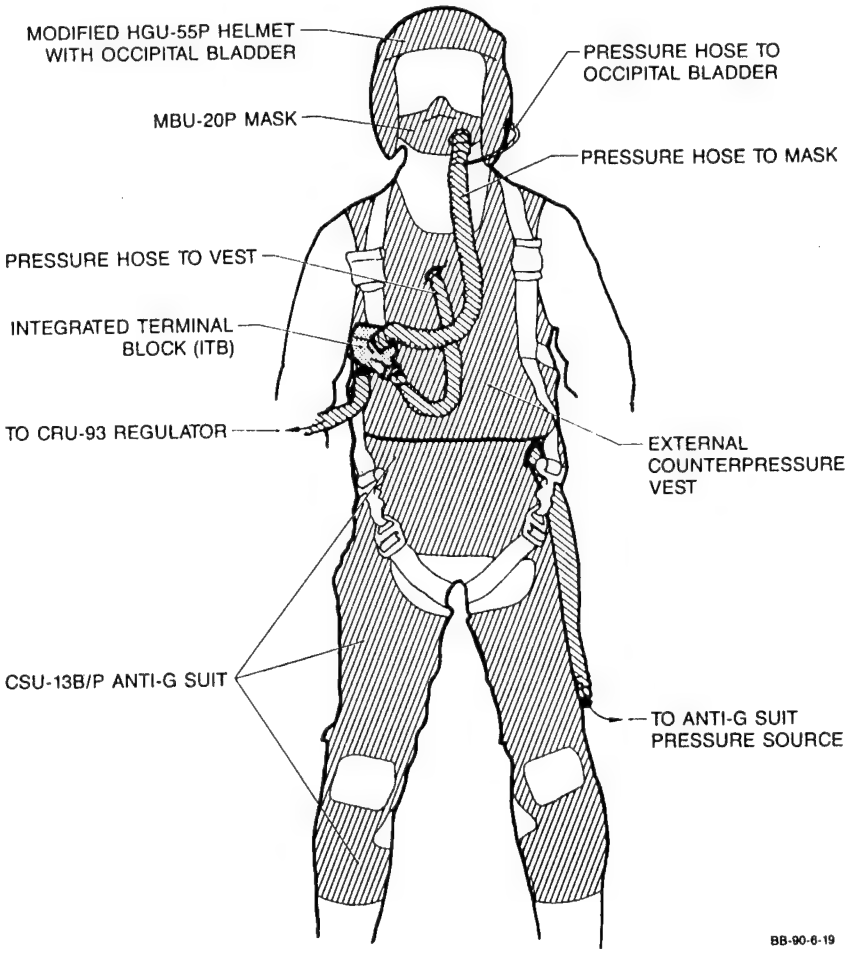
LIST OF TABLES

THIS PAGE LEFT BLANK INTENTIONALLY

INTRODUCTION

A new positive pressure breathing system for G-protection known as COMBAT EDGE is currently being evaluated for use in both the USAF and NAVY F-16 and the USAF F-15 aircraft. This system is being used in conjunction with the current Air Force standard CSU-13 B/P anti-G suit or the new Advanced Technology Anti-G Suit (ATAGS) being developed by the Armstrong Laboratory. The COMBAT EDGE system is comprised of a low profile oxygen mask (MBU-20P), a HGU-55P helmet modified with an occipital bladder used as a tensioning device for the mask, a counterpressure vest, and an integrated terminal block which connects both the oxygen mask and the counterpressure vest to the breathing regulator (Figure 1). COMBAT EDGE has been shown to enhance a pilots endurance to sustained acceleration.

Figure 1
COMBAT EDGE G PROTECTION SYSTEM



If this system is fully deployed, pilots can be safely exposed to a high time duration dose of positive pressure breathing over the course of a 20 year flying career. Recent concerns in this area raised by the Aerospace Medical Community have dealt primarily with the possibility of physiological effects of long duration exposure to PPB manifesting themselves into occupational health risks. To be more precise, these questions have centered around possible cardiopulmonary physiological effects of PPB.

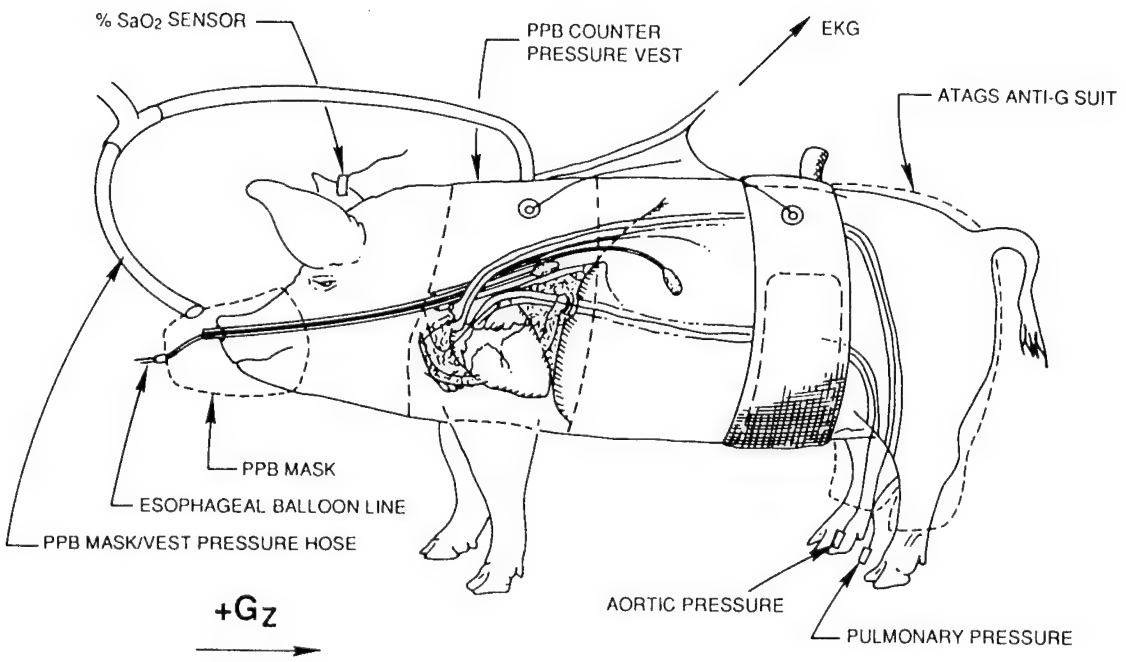
From a historical perspective, PPB has been used extensively by both the Royal Air Force in Britain and by the United States Air Force over the past 40 years to protect pilots from the physiological effects of altitude. Ackles (1) described the use of PPB by Britain's Royal Air Force for high altitude protection. It is important to point out that the levels of PPB used for altitude protection are lower (30 mm Hg maximum), than those proposed for G-protection (60 mm Hg maximum).

To address the question of potential occupational health risk effects from PPB, the Armstrong Laboratory has conducted two separate experiments to investigate both short and chronic exposure to PPB. In 1991, Burns et al. (2) reported the results of a study conducted at Brooks AFB, TX which investigated the effects of short duration exposure to PPB using the swine as the experimental test animal. Results from this study showed no significant physiologic findings. This report describes the follow-on PPB study conducted at the Armstrong Laboratory, Wright-Patterson AFB, OH, which examined chronic exposure to PPB. Swine were, again, used in order to enable researchers to compare results of the two studies. The miniature swine was selected as the human analog in this study because the animal's cardiopulmonary vasculature is very similar to that of a human. In addition, the swine will perform a natural, rhythmic straining maneuver under G, much like a human who is trained to strain during exposure to G. Previous work has shown the swine to be an excellent analog of the human in studying the effects of high, sustained G (2, 3).

METHODS

Eight male unanesthetized Minihanford miniature swine were selected for the study. Four served as experimental test animals and four served as control animals. Ages ranged from 6 to 7 months. Of the four control animals, three were euthanized at age 12 months and the one remaining control served as a live control and was euthanized along with the experimental test animals. The four control animals also acted as controls for a second unrelated experiment which explains the differences in age between the test and control animals. Experimental test animals were exposed to high G on 27 separate test days.

Echocardiograms were performed on all of the experimental test animals pre and post experiment. Post experimental echocardiograms were performed on the one live control only.



Instrumentation: Figure 2
ANIMAL INSTRUMENTATION

Instrumentation: Blood pressure recording catheters were surgically positioned in each of the four test animals prior to and following the 90 day test period (test days 1 and 27). General surgical anesthesia for the procedure was provided using a mixture of Isoflorthane and nitrous oxide. Prior to the initial G exposure test day 1, a 2 French Milar catheter and 7 French Swan-Ganz catheter were introduced into the animal's vascular system through an incision in the right femoral vein (Figure 2). The catheters were advanced anteriorly through the animal's right heart and into the pulmonary artery. Similarly, a 5 French Milar catheter was inserted into the femoral artery of the same limb and the tip advanced into the area of the aortic arch. Final placement of both catheters was accomplished under fluoroscopy. Prior to the final G exposure, test day 27, the above catheterization procedures were repeated. Vascular access in this instance being gained through vessels in the animal's left and right rear limbs.
The distal ends of both Milar catheters were attached to Milar TC-510 control units (Model SPC-3505-F). The Swan-Ganz catheter was connected to an American Edwards Laboratories

Cardiac Output computer (Model COM-1-RS). Both of these units were mounted on the animal platform of the centrifuge. Also mounted on this platform was a remotely activated infusion syringe capable of injecting iced saline through the thermal dilution port of the Swan-Ganz catheter. This experimental preparation allowed investigators to simultaneously record pulmonary artery pressure, aortic artery pressure, and cardiac output at various G levels while the animals were exposed to positive pressure breathing.

In addition to the above invasive procedures, pre and post experimental echocardiograms were obtained on each of the test animals. The pigs were anesthetized with Ketamine HCL (20 mg/kg) during these procedures. An Irex echocardiograph was used to obtain the recordings.

During each of the 27 centrifuge procedures, Baxter pre-gelled ECG electrodes attached to each side of the thorax and one attached to the lumbar area of the animal's back, enabled the continuous recording of the heart rate and electrocardiographic activity. An OMEGA 0-5 PSIG pressure transducer (model PX143-05 BG 5V) connected to the oxygen mask was used to record inspiratory and expiratory pressures was well as respiratory rate. A similar OMEGA 0-15 PSIG transducer (model PX142-015 G 5V) monitored anti-G suit pressure.

G-Protective Equipment: Human exposure to PPB was simulated in the pig by fitting each animal with a custom made PPB mask, counterpressure vest, and a full coverage anti-G suit similar in design to the prototype ATAGS (Figure 3.). Preliminary studies employing this equipment revealed that full coverage ATAGS induced severe respiratory difficulty in the subject animals when inflated to maximum pressure. This problem was solved by assuring that the ATAGS did not extend over the animal's ribs and by limiting the G suit pressure to 6 psi rather than 10 to 11 psi. Different pneumatic pressures in the mask and counter pressure vest versus that in the ATAGS were obtained using a tandem G-valve setup. One Alar valve was set at a 90 degree angle to the G vector which provided a maximum of 11 psi to the Tactical Life Support breathing regulator (Garrett Corporation serial number 31307-1) and the counterpressure vest. A second Alar G-valve was offset 45 degrees from the G vector thus assuring a maximum of 6 psi ATAGS pressure. This G-valve arrangement provided 55-60 mm Hg positive pressure to the mask.

Once instrumented and fitted with a mask and suit, the fully conscious pig was placed on the animal platform of the centrifuge (Figure 4). This device, also known as the Dynamic Environment Simulator, is used for both animal and human acceleration research. The animal platform is 20.5 feet from the center of rotation.

G-Profiles: Acceleration exposures consisted of a 10 minute 5 to 9 +Gz simulated aerial combat maneuver with 10 second plateaus at both +5 and +9 Gz. A 0.5G/second onset rate was used for all G exposures. G vectors and position of the animals during acceleration are illustrated in Figure 5.

Necropsy Procedures: Three of the four swine (#621 622 and 623), acted as controls for two separate experiments; this resulted in the animals being euthanized 5 months prior to the

completion of this study. Hearts and lungs were immersed in buffered formalin and retained for measuring gross perimeters and histopathologic examination after the four experimental animals and one live control were euthanized.

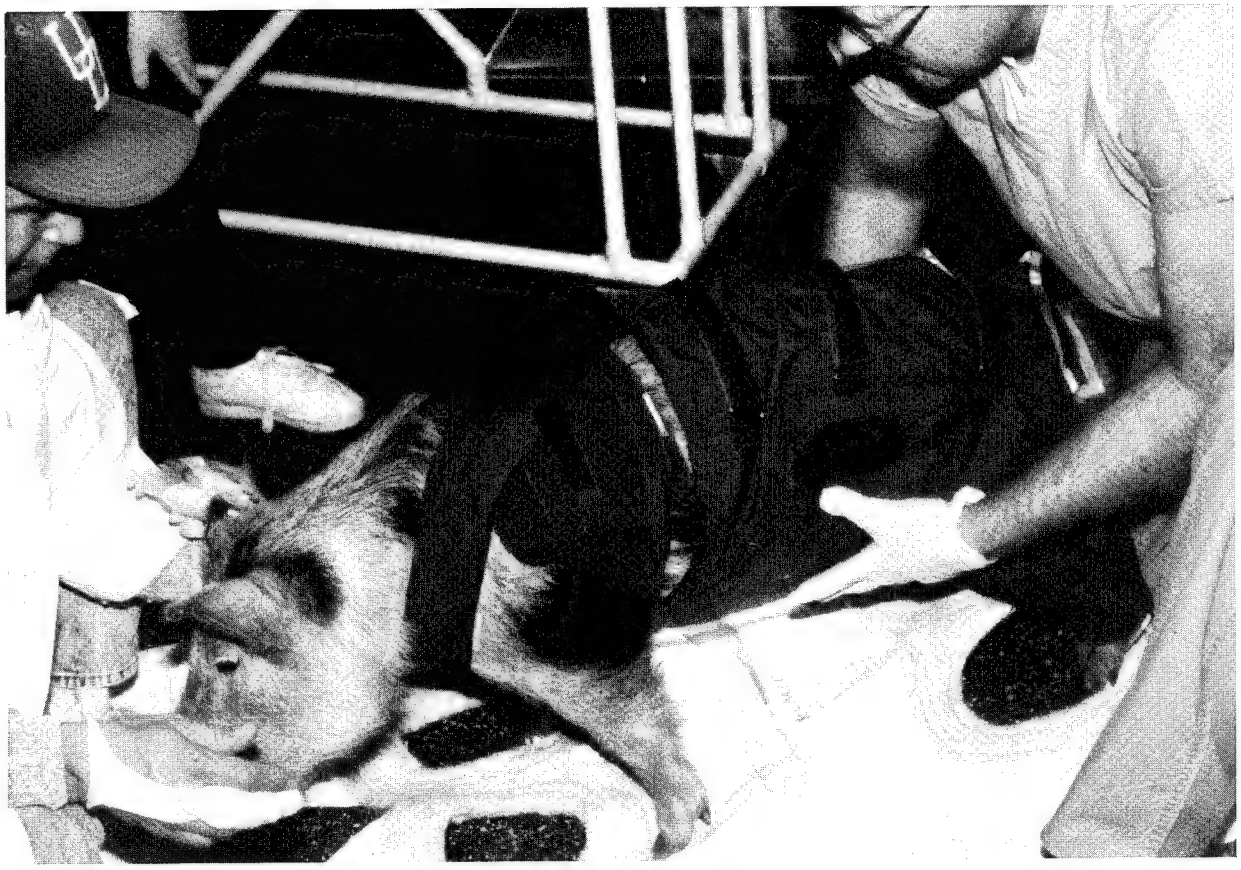


Figure 3
ANIMAL WEARING THE PPB G-SUIT ENSEMBLE

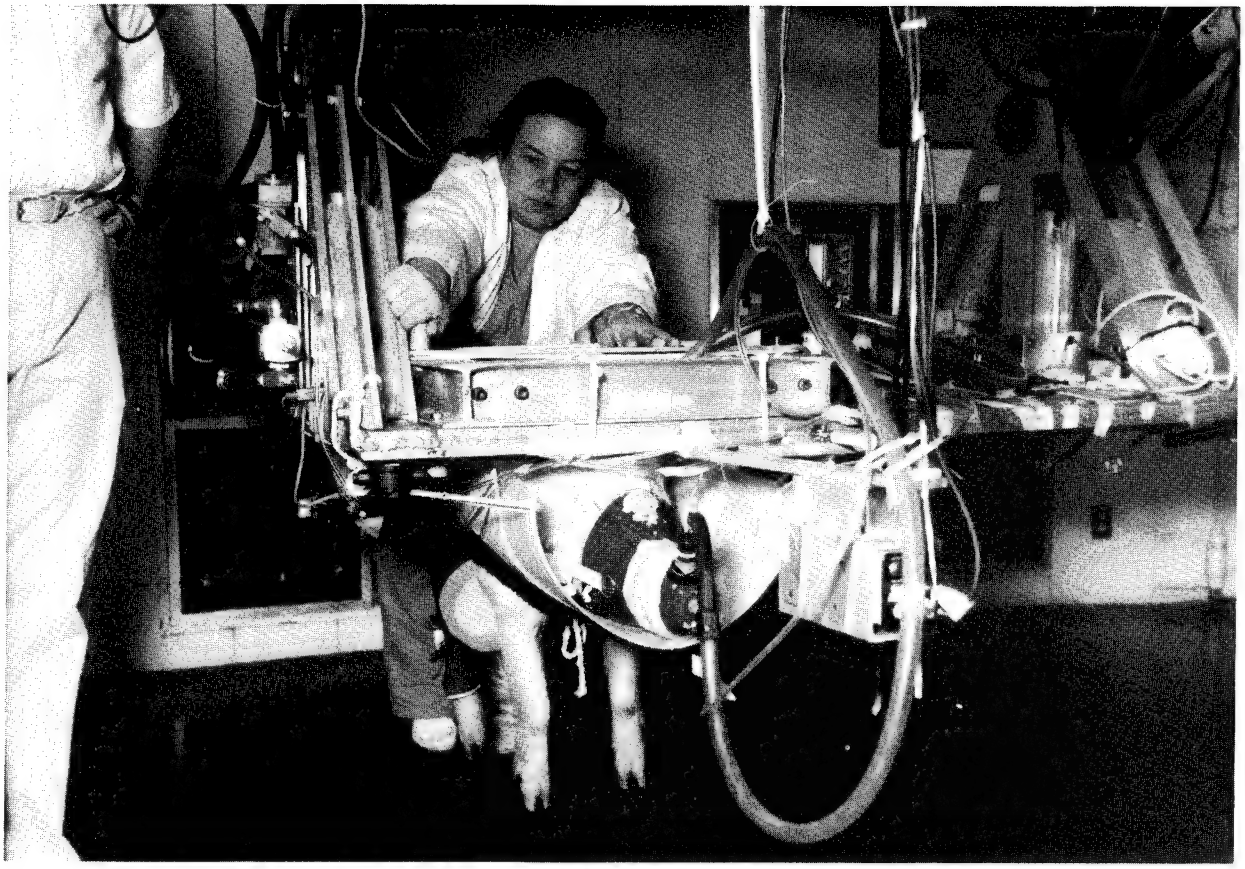


Figure 4
CENTRIFUGE ANIMAL PLATFORM

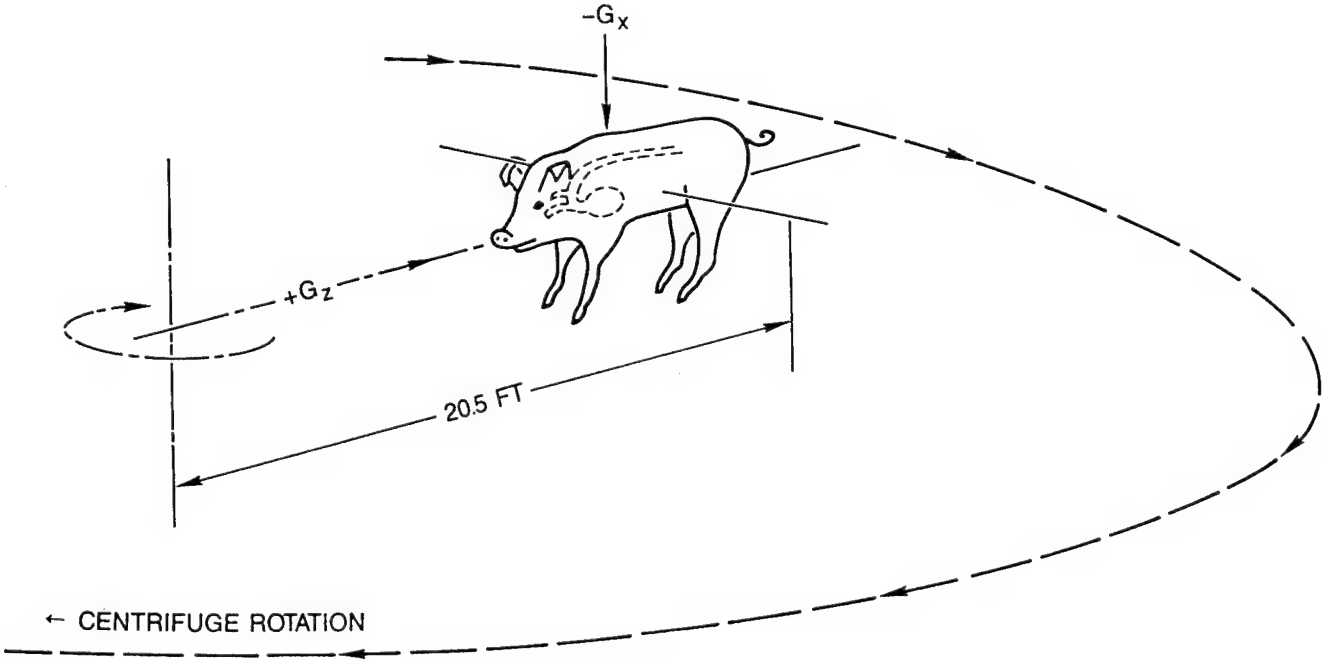


Figure 5
ANIMAL POSITION AND G VECTORS

The five remaining swine were anesthetized with ketamine hydrochloride, maintained in a surgical plane of anesthesia with sodium penobarbital as needed, and were perfused with 1% glutaraldehyde and 4% formaldehyde mixture 4CF-1G, McDowell, 1976 (3), via the abdominal aorta. The lungs were also perfused via the trachea with buffered formalin. The hearts and lungs were retained in 4CF-1G. Additional tissue (see gross examination) were retained in buffered formalin. The hearts from these 5 pigs were weighed, trimmed, and dissected into individual chambers and reweighed 48 hours after necropsy. The three other control hearts were similarly prepared. All tissues were paraffin embedded, sectioned at 3 microns, and stained with hematoxylin and eosin for routine histopathologic examination.

Data Collection: Mask pressure, heart rate, aortic pressure, pulmonary artery pressure, and respiration were sampled at a rate of 100 Hz and stored on computer disk. In addition, real time stripchart recordings were made of the G-level, EKG, aortic pressure, pulmonary artery pressure, mask pressure, respiration and percent arterial oxygen saturation. Cardiac output

data were manually recorded from the cardiac output device via a video picture of the cardiac output monitor's LED read out which was provided by a remote camera mounted on the animal platform of the centrifuge.

Statistical Analysis: Paired T-tests were used to compare data collected on day one versus day 27 of the experimental period.

RESULTS

Of all the parameters monitored, only mean aortic pressure recorded on day 27 at +9 Gz differed significantly from day 1 baseline levels ($p < 0.05$). Although not statistically significant, of interest is the fact that pulmonary artery pressure in three of the animals tested reached 120 mm Hg during the +9 G acceleration. Missing pulmonary artery pressure data for animal 152-5 was caused by the loss of arterial patency. In addition, day 1 data collection on animals 159-5 and 159-6 stopped abruptly due to the animals experiencing gravity induced loss of consciousness (Figure 6). Other data collected and analyzed are shown in the following figures: respiratory rate (Figure 7), cardiac output (collected only during +9 G peaks; equipment failure was responsible for not obtaining day 1 cardiac output data on animal 159-5, Figure 8), heart rate (Figure 9), and aortic pressures (Figure 10). Data along the x-axis in Figures 6 through 10 illustrate the various physiological data collected at both +5 and +9 Gz. This axis also depicts the various physiological parameters for each of the sixteen +9 Gz plateaus. The +5 to +9 G SACM lasted for 10 minutes in duration.

Echocardiographic Analysis: Of the 25 different echocardiographic measurements taken on each animal, no abnormal physiologic or morphologic changes were observed. There was, however, an increase in pulmonary artery velocity in all experimental animals. Mean pulmonary artery velocities for day 1 were 72.25 cm/sec, compared to day 27 with mean pulmonary velocities of 117.00 cm/sec. The 44.75 cm/sec change observed in these values does not exceed the upper limits of normal for these animals (Bonaguri, 1992) (see Appendix A). Although pulmonary artery blood flows appear to be elevated in comparison to the pre-baseline values, these values are within normal limits for the pulmonary artery. Echocardiographic data are graphically illustrated in Appendix B.

Gross Examination: Gross necropsies were conducted on each animal. Histologic examinations were performed on the following tissue: lungs, heart, liver, gallbladder, kidneys, adrenals, brain, and eyes of both the control and experimental animals. All animals were reported to be in excellent physical and nutritional condition prior to necropsy. Gross examination findings did reveal an increase in the mass of the left atrium in all test animals (Table 1 and 2).

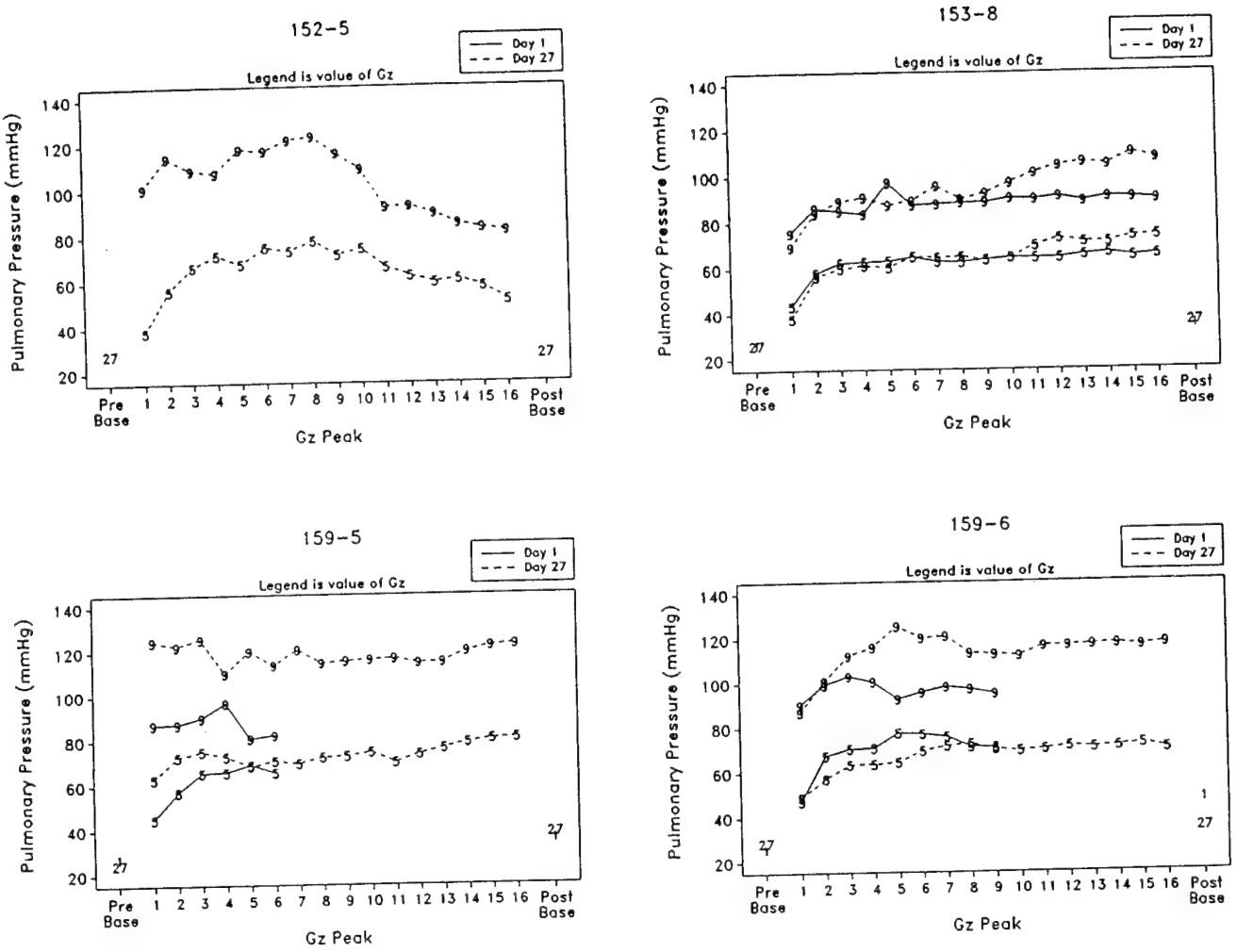
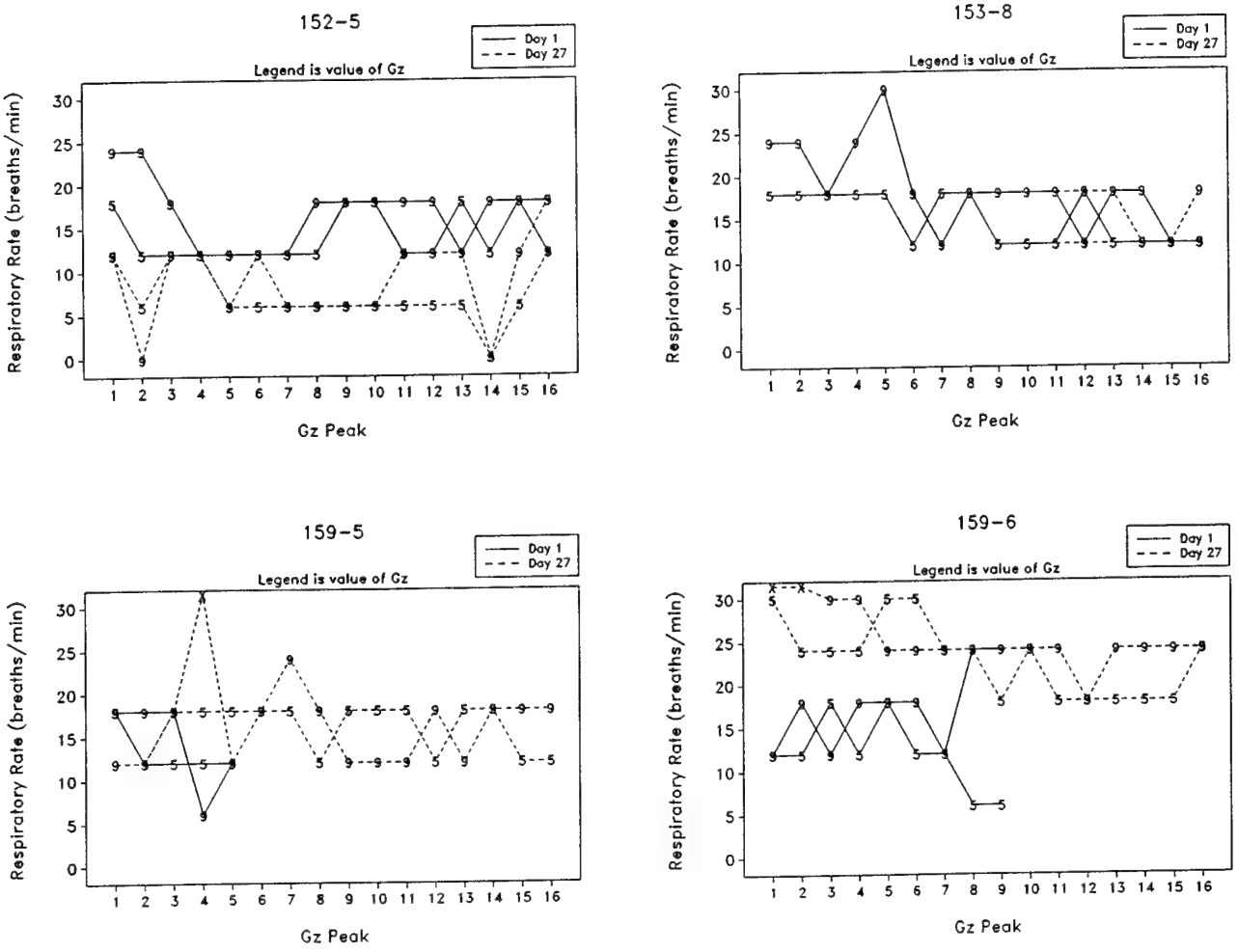


Figure 6
PULMONARY ARTERY PRESSURE
(N=4)



X indicates Rate > 32

Figure 7
RESPIRATORY RATE
(N=4)

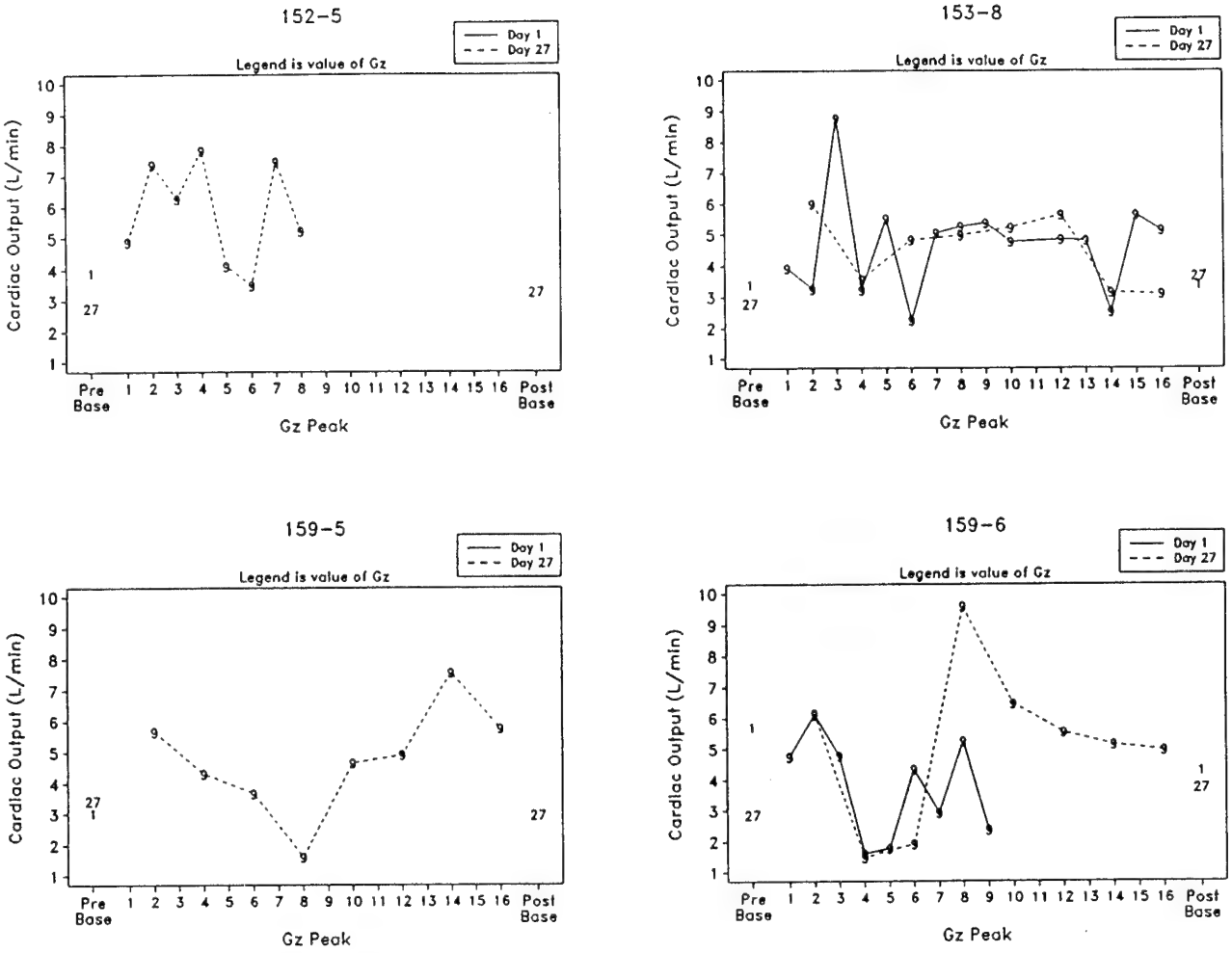


Figure 8
CARDIAC OUTPUT
(N=4)

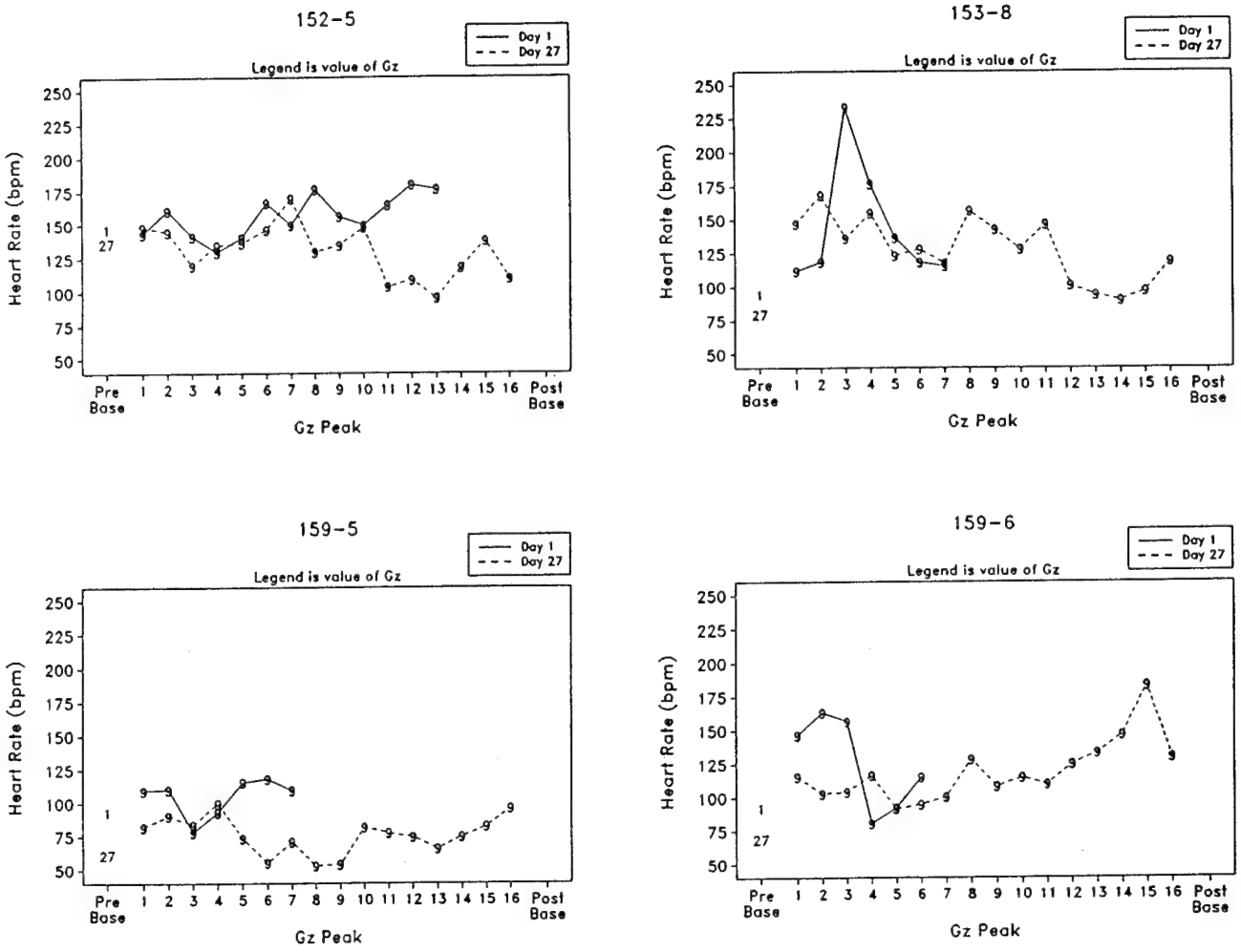


Figure 9
HEART RATE
(N=4)

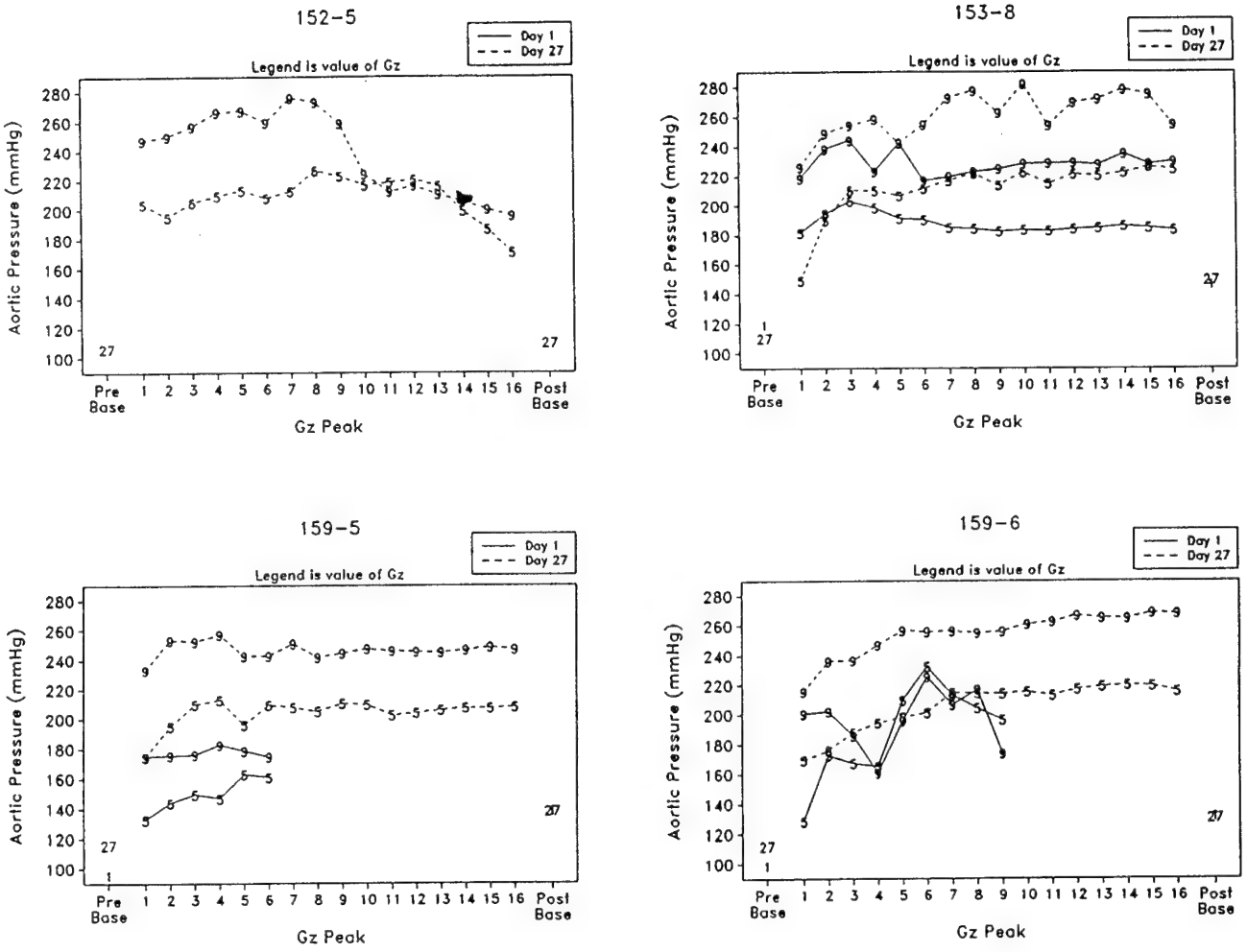


Figure 10
AORTIC
PRESSURE
(N=4)

Table 1
GROSS EXAMINATION OF TEST ANIMAL HEARTS

PIG NUMBER	450	451	452	453
BODY WT (Kg)	45.4	38.6	33.0	40.0
HEART FIXED (gm)	177.8	154.6	126.9	184.1
		HEART TRIMMED (gm)		
LT ATRIUM	11.1	12.3	11.4	9.7
RT ATRIUM	12.9	10.5	9.8	11.2
LT VENT & SEP	107.5	94.0	79.8	110.1
RT VENT	34.6	27.7	21.8	43.0
TOTAL WT	166.1	144.5	122.8	174.0
		MASS RATIOS		
HEART/BODY WT	0.37	0.37	0.37	0.43
RT VENT/HEART	0.21	0.19	0.18	0.25

Table 2
GROSS EXAMINATION OF CONTROL ANIMAL HEARTS

PIG NUMBER	44-8	48-6	65-4	65-7
BODY WT (Kg)	44.6	33.8	38.0	34.4
HEART FIXED (gm)	199.8	134.0	164.4	149.2
		HEART TRIMMED (gm)		
LT ATRIUM	9.2	5.8	7.0	8.6
RT ATRIUM	12.2	8.1	8.5	8.6
LT VENT & SEP	129.4	79.9	100.2	83.6
RT VENT	36.3	28.5	29.5	31.6
		MASS RATIOS		
HEART/BODY WT	0.42	0.36	0.38	0.38
RT VENT/HEART	0.19	0.23	0.20	0.24

Histopathologic Examination: Tissue samples of control animals were obtained from the lungs, heart, aorta, and the pulmonary trunk. Heart mass, heart to body mass ratio, and right ventricle to heart ratio data for all animals are shown in Appendix B. Two of the four experimental animals showed a mild degree of fibrosis in the lung while none of the control animals including the live control showed any degree of lung fibrosis. All other tissue taken from other organs were essentially normal. Neither gross nor histopathlogical examination of the left atrial myocardium or mitral valve accounted for the increase in left atrial weight. The pathological findings are summarized in Appendix C.

DISCUSSION

The main objective of this study was to examine the cardiopulmonary effects of PPB following a simulated life time dose of PPB with high G for a typical Tactical Air Force fighter pilot. In recent years, the Aerospace Medical Community has voiced concerns pertaining to the longitudinal physiological effects of repeated exposure to PPB. One of the major concerns is that repeated exposure to high Gz will cause acute RV dilatation resulting in chronic dilatation and RV pathology. To better understand the effects of chronic exposure to maximum levels of PPB, this study was designed to apply the maximum level of PPB provided by current COMBAT EDGE regulators (60 mm Hg) at a G dose which would exceed that encountered in typical fighter pilot's career. As a result, each animal received over 400 -10 sec exposures to 60 mm Hg at +9 Gz. This equates to a total time of 66 minutes PPB/G dose exposure per animal. Echocardiographic and histopathological examination of the heart revealed no significant change in RV size or changes in tissue morphology. Human testing of COMBAT EDGE has resulted in some human exposures of over 10 minutes of the +5 to +9 G SACM on the Armstrong centrifuge at Brooks AFB, TX.

The chronic exposure of swine to positive pressure breathing or PPB has not presented any severe physiological consequences, however, there are some interesting observations in the area of aortic and pulmonary pressure tracings. There is a statistically significant difference in aortic pressures measured at +9 Gz on day 27 when compared to day 1 ($p < 0.0055$). Differences were also seen for the pulmonary pressures as well, however, these differences were not statistically significant. One explanation for these increases may be attributed to increased peripheral vascular resistance and vascular tone at day 27. The maximum aortic and pulmonary pressures from day 27 did not differ or exceed the maximum aortic and pulmonary pressures reported by Burns et al., 1991 (2). The use of extended coverage or ATAGS like anti-G suit in combination with PPB, has a profound effect on blood pressure in swine. This study showed dramatic increases in aortic peak pressure of 281 mm Hg (measured at the aortic arch) and peak pulmonary pressure of 125 mm Hg (measured in the pulmonary artery). These types of increases in cardiac blood pressures have also been reported in a study using miniature swine (2). Their findings showed that the combination of an extended coverage anti-G suit used in conjunction with PPB during exposures to +9 Gz produced peak left ventricular pressures of 352 mm Hg, peak right ventricular pressures of 163 mm Hg, mean arterial

systolic pressures of 305 mm Hg and mean diastolic pressures of 209 mm Hg.
Another interesting finding from this study was the increase in weight of the left atrium in the experimental test animals. This change occurred in spite of the fact that the histopathological examination of the tissue was essentially normal, and the echocardiographic measurements of the left atrium did not show a significant change in size to account for the weight increase. It is speculated that a larger N size may have brought left atrium weights within normal range. Mass ratios which compared heart to body weight and right ventricle to heart weight showed no significant difference when the mass ratios of the controls were compared to the mass ratios of the test animal population. Histopathological examination of the pulmonary trunk and aorta of both the control and test swine revealed circumferential, and multifocal dense fibrosis. These areas of fibrosis occurred at or near the pulmonic valve and were believed to be normal morphologic findings. In previous work by MacKenzie et al., 1976, (6), and Burton et al., 1976, (7), abnormal myocardial pathology in miniature swine exposed to sustained +Gz levels as high as +15 Gz. Gross and histopathologic examination of the test animal hearts found myofibrillar degeneration, lesions, cardiomyopathy, and subendocardial hemorrhage which were thought to be related to animal heart rates in excess of 200 bpm and an increase in the serum catecholamine levels. These same histopathologic changes were not seen in the current study. One reason for this may be related to the lower heart rates of animals used in this study. As Figure 9 shows heart rates in animals chronically exposed to +9 Gz remained below 200 bpm, with the exception of animal number 153-8 whose heart rate spiked above 225 bpm on the third +9 Gz plateau during day 1 of testing.

CONCLUSIONS

With the exception of increased aortic pressure, the results of chronic exposure to the maximum levels of PPB showed no dramatic effect on the function of the heart or changes in morphology such as hypertrophy of its chambers. In addition, there were no significant histopathologic changes observed upon microscopic examination of various tissues. There were however, increases in left atrial weight noted during gross examination of the heart however, this finding was not substantiated by echocardiographic or morphological changes in atrial tissue thickness. Additional insight into these data would require a more robust study using a larger animal population.

Long term medical tracking of F-16 pilots currently using COMBAT EDGE operationally has already been initiated. To date, there have been no reported aeromedical problems associated with the deployment of COMBAT EDGE. As those pilots who are protected with COMBAT EDGE are medically monitored throughout their careers, it is hoped that this research on an animal model of the human will contributed to a better understanding of the chronic effects of PPB and high G.

REFERENCES

1. Ackles, K.N., Porlier, J. A. G., Holness, D. E., Wright, G. R., Lambert, J. M., and McArthur, W. J. Protection against the physiological effects of positive pressure breathing, (1978), Aviat. Space and Environ. Med., 49(6):753-758.

2. Burns, J.W., Fanton, J.W., Desmond, J.L. Hemodynamic responses to positive pressure breathing during +Gz (PBG) in swine, (1991), Advisory Group For Aerospace Research & Development AGARD-CP-516, October 1991.

3. McDowell, E.M., Trump, B. F. Histologic fixative suitable for diagnostic light and electron microscopy. Arch Pathol Lab Med 100:405-414, 1976.

4. Bonaguri J. Personal Communication, July 1992.

5. Burton, R.R. Positive (+Gz) acceleration tolerance of the miniature swine: application as a human analog. (1973), Aerospace Med., 44(3):294-298.

6. MacKenzie, W.F., Burton, R.R., Butcher, W.I. Cardiac pathology associated with high sustained +Gz: II. Stress cardiomyopathy. (1976), Aviat. Space and Environ. Med., 47(7):718-725.

7. Burton, R.R., MacKenzie, W.F. Cardiac pathology associated with high sustained +Gz: I. subendocardial hemorrhage. (1976), Aviat. Space and Environ. Med. 47(7):711-717.

Echocardiographic Data In Numeric Format APPENDIX A

Pig#	Period	Pig#	Period	LA_2D	Aorta	RR_s	LVWd	LVIDd	IVSd	RVIDd	LVWs	LVIDs	IVSs	IVSamp	IVScv	RVWd	RA2D	PA	PA_vel	TV_E_vel	TV_A_vel	TR_vel	PI_vel	RA/LA	RVw/LVw	RVid/LVid	PA/Ao	LV_SF_%
65-7CTL	Baseline	65-7CTL	Baseline	3.25	1.86	0.88	0.56	3.95	0.68	1.57	1.18	2.58	1.06	0.66	Normal	0.23	3.19	1.51	66.30	49.30	35.30	neg	neg	0.98	0.41	0.40	0.81	32.97
159-6	Baseline	159-6	Baseline	3.78	2.19	0.61	0.56	3.67	0.79	1.16	1.51	1.81	1.37	1.04	Normal	0.35	2.48	1.69	77.00	79.30	33.30	neg	neg	0.66	0.62	0.32	0.77	31.77
159-5	Baseline	159-5	Baseline	3.33	1.87	1.15	0.48	3.92	0.74	0.64	1.05	2.69	1.18	0.31	Normal	0.24	2.72	1.53	55.60	67.00	41.70	neg	neg	0.82	0.50	0.16	0.82	32.34
153-8	Baseline	153-8	Baseline	3.14	2.37	0.82	0.49	3.28	0.80	1.10	0.97	2.29	1.07	0.42	Normal	0.23	2.56	1.76	90.70	61.70	42.70	alias	neg	0.82	0.47	0.34	0.74	25.82
152-5	Baseline	152-5	Baseline	3.81	2.26	0.62	0.54	3.96	0.80	0.76	0.95	3.03	1.16	0.37	Normal	0.34	2.94	1.85	65.70	58.30	34.00	neg	neg	0.77	0.63	0.19	0.82	31.95
65-4CTL	Baseline	65-4CTL	Baseline	4.43	2.52	0.87	0.59	4.25	0.91	1.48	1.09	2.85	1.11	0.39	Normal	0.33	2.81	1.83	72.30	61.00	40.30	neg	neg	0.63	0.56	0.35	0.73	35.79
48-6CTL	Baseline	48-6CTL	Baseline	3.66	2.18	0.97	0.58	4.27	0.67	1.26	0.71	3.31	0.85	0.31	Normal	0.23	3.28	1.84	68.70	77.70	34.00	neg	1.2 m/sec	0.90	0.40	0.30	0.84	34.95
152-5	Post	152-5	Post	4.28	2.67	1.09	0.89	5.79	1.15	1.68	1.36	4.43	1.43	0.54	Normal	0.35	2.94	1.81	125.00	98.00	55.30	neg	1.29 m/se	0.69	0.39	0.29	0.68	50.25
153-8	Post	153-8	Post	3.01	2.75	0.5	0.61	3.35	0.81	1.10	1.37	1.95	1.27	0.68	Normal	0.32	2.27	1.37	144.30	62.00	36.00	2.44 m/se	neg	0.75	0.52	0.33	0.50	27.68
159-5	Post	159-5	Post	4.19	2.31	0.71	0.53	3.91	1.03	0.92	1.01	2.78	1.31	0.42	Normal	0.30	3.09	1.48	78.00	ND	ND	neg	neg	0.74	0.57	0.24	0.64	31.99
13-7	Post	13-7	Post	4.17	3.07	0.66	0.66	4.21	0.86	1.57	1.19	3.19	1.23	0.53	Normal	0.33	2.93	1.92	59.70	34.70	38.70	neg	neg	0.70	0.50	0.37	0.63	34.52
159-6	Post	159-6	Post	3.45	2.47	0.76	0.65	4.46	0.79	1.20	1.33	2.62	1.31	0.60	Normal	0.38	3.19	1.77	120.70	115.70	82.30	alias	neg	0.92	0.58	0.27	0.72	38.73
Mean	Base(n=7)	Mean	Base(n=7)	3.63	2.18	0.85	0.54	3.90	0.77	1.14	1.07	2.65	1.11	0.50	Normal	0.28	2.85	1.72	70.90	64.90	37.33	------	-----	0.79	0.51	0.29	0.79	32.23
Mean	Post(n=5)	Mean	Post(n=5)	3.82	2.65	0.74	0.67	4.34	0.93	1.29	1.25	2.99	1.31	0.59	Normal	0.34	2.88	1.67	105.54	82.08	42.46	-----	-----	0.75	0.50	0.30	0.63	36.63

PATHOLOGY CLINICAL RECORD						ACCESSION NO. 448-92
T.D.NO.	ANIMAL NO.	DATE DIED	DEPT.	SEX	DISP.	CONDITION
005	13-7	NA	THV	M	A	G

SPECIES	STRAIN	SOURCE NEC. NO.	ORIGIN	INVESTGATOR
PIG	NA	NA	AF	COOPER

AGENT	CONCENTRATION	EUTHANASIA	NEC. DATE	TIME DIED
NA	NA	PENTABARB	17MAR92	NA

GENERAL CONDITION GOOD, FAIR, POOR, THIN, EMAC., OTHER,	X FOR TISSUE TAKEN	X FOR EXAM MICRO.

GROSS EXAMINATION

This pig is in excellent physical and nutritional condition. The only observed lesion is multifocal minimal subendocardial hemorrhage; this lesion is believed to be attributed to perfusion. Animal weights and organ weights and measurements are on a separate attached sheet. Organ weights were rounded to the nearest tenth of a gram.

HISTOPATHOLOGIC EXAMINATION

Diffusely within the right ventricle in the section nearest the valve there is prominent subendocardial fibrous thickening with fibrosis extending into the underlying myocardium. This thickening is more pronounced than in any treatment animal with the exception of pig 451.

Focally within the trachea and rarely surrounding the pulmonary airways are small aggregates of lymphocytes.

Gary B Marit

GARY B. MARIT, MAJ, VC, USA
Army/Medical Research Unit
Toxicology Division

3 April 1992

	NASAL SECTION
	BONE
	BONE MARROW
	TRACHEA
	LARYNX
	ESOPHAGUS
	THYROID
	PARATHYROIDS
X	LUNGS
X	HEART
X	LIVER
X	GALLBLADDER
X	SPLEEN
	THYMUS
	MAND. LYMPH ND.
	MEST. LYMPH ND.
X	KIDNEYS
X	ADRENALS
	SALIVARY GLAND
	URIN. BLADDER
	STOMACH
	DUODENUM
	PANCREAS
	JEJUNUM
	ILEUM
	COLON
	ANUS
	TESTES/OVARIES
	SEM.VES./UTERUS
	PROSTATE/VAGINA
	SKIN
	MUSCLE
	NERVE
	MAMMARY GLAND
	PITUITARY
	BRAIN
X	BRAIN
X	EYES

PRO.	GM TRIM	EMB	R.O.	H.T.
GM/PP/JN	17	17		SLW

SIGNATURE Gary Nicholson DATE 27 Mar 92

PATHOLOGY CLINICAL RECORD						ACCESSION NO. 621-92
T.D.NO. 005	ANIMAL NO. 48-6	DATE DIED 10/31/91	DEPT. VS	SEX M	DISP. A	CONDITION G
SPECIES SWINE	STRAIN HAN.	SOURCE NEC. NO. NA	ORIGIN OEVM	INVESTGATOR DR. COOPER		
AGENT NA	CONCENTRATION CONTROL	EUTHANASIA ?	NEC. DATE 10/3/91	TIME DIED NA		

GENERAL CONDITION GOOD, FAIR, POOR, THIN, EMAC., OTHER,		X FOR TISSUE TAKEN	X FOR EXAM MICRO.
CONTROL ANIMAL ON PPB STUDY			NASAL SECTION
			BONE
			BONE MARROW
			TRACHEA
			LARYNX
			ESOPHAGUS
			THYROID
Histopathologic examination revealed essentially normal tissue.			PARATHYROIDS
		X	LUNGS
		X	HEART
			LIVER
			GALLBLADDER
			SPLEEN
			THYMUS
			MAND. LYMPH ND.
			MEST. LYMPH ND.
			KIDNEYS
			ADRENALS
			SALIVARY GLAND
			URIN. BLADDER
			STOMACH
			DUODENUM
			PANCREAS
			JEJUNUM
			ILEUM
			COLON
			ANUS
			TESTES/OVARIES
			SEM.VES./UTERUS
			PROSTATE/VAGINA
			SKIN
			MUSCLE
			NERVE
			MAMMARY GLAND
			PITUITARY
			BRAIN
		X	AORTA
		X	PULMONARY TRACT

Mary B Marit

GARY B. MARIT, MAJ, VC, USA
Army Medical Research Unit
Toxicology Division

30 April 1992

PRO.	TRIM	EMB	R.O.	H.T.
DR. M	MM	QPP		SLW

SIGNATURE Jerry Nicholson DATE 21APR92

PATHOLOGY CLINICAL RECORD						ACCESSION NO. 623-92
T.D.NO. 005	ANIMAL NO. 65-7	DATE DIED 10/31/91	DEPT. VS	SEX M	DISP. A	CONDITION G
SPECIES SWINE	STRAIN HAN.	SOURCE NEC. NO. NA		ORIGIN OEVM		INVESTGATOR DR. COOPER
AGENT NA	CONCENTRATION CONTROL	EUTHANASIA ?		NEC. DATE 10/31/91		TIME DIED NA
GENERAL CONDITION GOOD, FAIR, POOR, THIN, EMAC., OTHER,					X FOR TISSUE TAKEN	X FOR EXAM MICRO.

CONTROL ANIMAL ON PPB STUDY

Histopathologic examination revealed essentially normal tissue

Gary B Marit

GARY B MARIT, MAJ, VC, USA
Army Medical Research Unit
Toxicology Division

30 April 1992

	X	
NASAL SECTION		
BONE		
BONE MARROW		
TRACHEA		
LARYNX		
ESOPHAGUS		
THYROID		
PARATHYROIDS		
LUNGS	X	
HEART	X	
LIVER		
GALLBLADDER		
SPLEEN		
THYMUS		
MAND. LYMPH ND.		
MEST. LYMPH ND.		
KIDNEYS		
ADRENALS		
SALIVARY GLAND		
URIN. BLADDER		
STOMACH		
DUODENUM		
PANCREAS		
JEJUNUM		
ILEUM		
COLON		
ANUS		
TESTES/OVARIES		
SEM. VES./UTERUS		
PROSTATE/VAGINA		
SKIN		
MUSCLE		
NERVE		
MAMMARY GLAND		
PITUITARY		
BRAIN		
AORTA	X	
PULMONARY TRUNK	X	

PRO.	TRIM	EMB	R.O.	H.T.
?	DR. M 9	9PP		SLW

SIGNATURE Jerry Nicholson DATE 21 Apr 92

PATHOLOGY CLINICAL RECORD						ACCESSION NO. 622-92
T.D.NO. 005	ANIMAL NO. 65-4	DATE DIED 10/31/91	DEPT. VS	SEX M	DISP. A	CONDITION G
SPECIES SWINE	STRAIN HAN.	SOURCE NEC. NO. NA	ORIGIN OEVM	INVESTGATOR DR. COOPER		
AGENT NA	CONCENTRATION CONTROL	EUTHANASIA ?	NEC. DATE 10/31/91	TIME DIED NA		
GENERAL CONDITION GOOD, FAIR, POOR, THIN, EMAC., OTHER,				X FOR TISSUE TAKEN	X FOR EXAM MICRO.	

CONTROL ANIMAL ON PPB STUDY

Histopathologic examination revealed essentially normal tissue.

	NASAL SECTION	
	BONE	
	BONE MARROW	
	TRACHEA	
	LARYNX	
	ESOPHAGUS	
	THYROID	
	PARATHYROIDS	
X	LUNGS	
X	HEART	
	LIVER	
	GALLBLADDER	
	SPLEEN	
	THYMUS	
	MAND. LYMPH ND.	
	MEST. LYMPH ND.	
	KIDNEYS	
	ADRENALS	
	SALIVARY GLAND	
	URIN. BLADDER	
	STOMACH	
	DUODENUM	
	PANCREAS	
	JEJUNUM	
	ILEUM	
	COLON	
	ANUS	
	TESTES/OVARIES	
	SEM.VES./UTERUS	
	PROSTATE/VAGINA	
	SKIN	
	MUSCLE	
	NERVE	
	MAMMARY GLAND	
	PITUITARY	
	BRAIN	
X	AORTA	
X	PULMONARY TRUNK	

Gary B. Marit

GARY B. MARIT, MAJ, VC, USA
Army Medical Research Unit
Toxicology Division

30 April 1992

PRO.	TRIM	EMB	R.O.	H.T.
?	DR.M 9	9 PP		SLW

SIGNATURE Jerry Nicholson DATE 21 Apr 92

PATHOLOGY CLINICAL RECORD						ACCESSION NO. 450-92
T.D.NO. 005	ANIMAL NO. 152-5	DATE DIED NA	DEPT. THV	SEX M	DISP. A	CONDITION G
SPECIES PIG	STRAIN NA	SOURCE NEC. NO. NA	ORIGIN AF	INVESTGATOR COOPER		
AGENT NA	CONCENTRATION NA	EUTHANASIA PENTABARB	NEC. DATE 18MAR92	TIME DIED NA		
GENERAL CONDITION GOOD, FAIR, POOR, THIN, EMAC., OTHER,				X FOR TISSUE TAKEN	X FOR EXAM MICRO.	

GROSS EXAMINATION

This pig is in excellent physical and nutritional condition. The only observed lesion is a nodular swelling approximately 7 cm in diameter on the medial aspect of the right thigh. This is the sight of a study related surgical procedure approximately 10 days prior to necropsy. Animal weights and organ weights and measurements are on a separate attached sheet. Organ weights were rounded to the nearest tenth of a gram.

HISTOPATHOLOGIC EXAMINATION

1. Myocardium; right ventricular free wall: Fibrosis, multifocal, mild.

2. Proximal pulmonary trunk: Fibrosis, focal, moderate.

3. Lung: Lymphoid aggregates, multifocal, minimal to mild.

4. Lung: Fibrosis, interstitial, multifocal, minimal.

COMMENT:

The most significant finding is focal subendothelial fibrosis in the pulmonary trunk as it leaves the heart. There is within the mid-myocardium of the right ventricle multifocal fibrosis.

		NASAL SECTION				
		BONE				
		BONE MARROW				
		TRACHEA				
		LARYNX				
		ESOPHAGUS				
		THYROID				
		PARATHYROIDS				
X		LUNGS				
X		HEART				
X		LIVER				
X		GALLBLADDER				
X		SPLEEN				
		THYMUS				
		MAND. LYMPH ND.				
		MEST. LYMPH ND.				
X		KIDNEYS				
X		ADRENALS				
		SALIVARY GLAND				
		URIN. BLADDER				
		STOMACH				
		DUODENUM				
		PANCREAS				
		JEJUNUM				
		ILEUM				
		COLON				
		ANUS				
		TESTES/OVARIES				
		SEM. VES./UTERUS				
		PROSTATE/VAGINA				
		SKIN				
		MUSCLE				
		NERVE				
		MAMMARY GLAND				
		PITUITARY				
X		BRAIN				
X		EYES				

PRO. GM/PP/JN	TRIM	EMB	R.O.	H.T.
	JWY 17	JWY 17		SLW

SIGNATURE Jerry Nicholson DATE 24 Nov 92

The pulmonary fibrosis is subjectively more pronounced in this animal than any other pig. However, the difference is minimal and it may be within normal limits. The pulmonary lymphoid aggregates are slightly larger, but much more common than observed in the control.

Gary B Marit

GARY B. MARIT, MAJ, VC, USA
Army Medical Research Unit
Toxicology Division
3 April 1992

PATHOLOGY CLINICAL RECORD						ACCESSION NO. 451-92
T.D.NO. 005	ANIMAL NO. 159-5	DATE DIED NA	DEPT. THV	SEX M	DISP. A	CONDITION G
SPECIES PIG	STRAIN NA	SOURCE NEC. NO. NA		ORIGIN AF		INVESTGATOR COOPER
AGENT NA	CONCENTRATION NA	EUTHANASIA PENTABARB		NEC. DATE 18MAR92		TIME DIED NA
GENERAL CONDITION GOOD, FAIR, POOR, THIN, EMAC., OTHER,				X FOR TISSUE TAKEN		X FOR EXAM MICRO.

GROSS EXAMINATION

This pig is in excellent physical and nutritional condition. The only observed lesion is multifocal minimal subendocardial hemorrhage; this lesion is believed to be attributed to perfusion. In addition, this animal had a surgical sight similar to pig #450. Animal weights and organ weights and measurements are on a separate attached sheet. Organ weights were rounded to the nearest tenth of a gram.

HISTOPATHOLOGIC EXAMINATION

1. Heart: Subendocardial fibrosis, diffuse, mild to moderate.

2. Proximal pulmonary trunk: Fibrosis, multifocal, moderate.

3. Lung: Lymphoid aggregates, multifocal, minimal to mild.

COMMENT:

The subendocardial fibrosis tends to be limited primarily to the right ventricle. The thickness is greater than the control pig and the fibrosis does not extend into the underlying myocardium. The lung and pulmonary trunk lesions are similar to those described with pig 450-92.

Gary B. Marit

GARY B. MARIT, MAJ, VC, USA
Army Medical Research Unit
Toxicology Division

3 April 1992

	NASAL SECTION
	BONE
	BONE MARROW
	TRACHEA
	LARYNX
	ESOPHAGUS
	THYROID
	PARATHYROIDS
X	LUNGS
X	HEART
X	LIVER
X	GALLBLADDER
X	SPLEEN
	THYMUS
	MAND. LYMPH ND.
	MES. LYMPH ND.
X	KIDNEYS
X	ADRENALS
	SALIVARY GLAND
	URIN. BLADDER
	STOMACH
	DUODENUM
	PANCREAS
	JEJUNUM
	ILEUM
	COLON
	ANUS
	TESTES/OVARIES
	SEM.VES./UTERUS
	PROSTATE/VAGINA
	SKIN
	MUSCLE
	NERVE
	MAMMARY GLAND
	PITUITARY
X	BRAIN
X	EYES

PRO.	TRIM	EMB	R.O.	H.T.
GM/PP/JN	GM 17	17		GM 11 APR 92

SIGNATURE Gary B. Marit DATE 3 APR 92

PATHOLOGY CLINICAL RECORD						ACCESSION NO. 452-92
T.D.NO.	ANIMAL NO.	DATE DIED	DEPT.	SEX	DISP.	CONDITION
005	153-8	NA	THV	M	A	G

SPECIES	STRAIN	SOURCE NEC. NO.	ORIGIN	INVESTGATOR
PIG	NA	NA	AF	COOPER

AGENT	CONCENTRATION	EUTHANASIA	NEC. DATE	TIME DIED
NA	NA	PENTABARB	18MAR92	NA

GENERAL CONDITION GOOD, FAIR, POOR, THIN, EMAC., OTHER,		X FOR TISSUE TAKEN	X FOR EXAM MICRO.

GROSS EXAMINATION

This pig is in excellent physical and nutritional condition. The only observed lesion is a nodular swelling approximately 7 cm in diameter on the medial aspect of the right thigh. This is the sight of a study related surgical procedure approximately 10 days prior to necropsy. Animal weights and organ weights and measurements are on a separate attached sheet. Organ weights were rounded to the nearest tenth of a gram.

During tissue trimming on 26 March a 0.5x0.2cm yellow gritty nodule was observed on the ventral edge of the right medial lung lobe.

HISTOPATHOLOGIC EXAMINATION

1. Distal aorta: Mineralization, multifocal, mild.

2. Lung: Pyogranuloma, focal, moderate.

3. Lung: Lymphoid aggregates, multifocal, minimal to mild.

4. Lung: Fibrosis, multifocal, mild.

5. Proximal pulmonary trunk: Fibrosis, focal, segmental, mild.

		NASAL SECTION		
		BONE		
		BONE MARROW		
		TRACHEA		
		LARYNX		
		ESOPHAGUS		
		THYROID		
		PARATHYROIDS		
X		LUNGS		
X		HEART		
X		LIVER		
X		GALLBLADDER		
X		SPLEEN		
		THYMUS		
		MAND. LYMPH ND.		
		MES. LYMPH ND.		
X		KIDNEYS		
X		ADRENALS		
		SALIVARY GLAND		
		URIN. BLADDER		
		STOMACH		
		DUODENUM		
		PANCREAS		
		JEJUNUM		
		ILEUM		
		COLON		
		ANUS		
		TESTES/OVARIES		
		SEM.VES./UTERUS		
		PROSTATE/VAGINA		
		SKIN		
		MUSCLE		
		NERVE		
		MAMMARY GLAND		
		PITUITARY		
X		BRAIN		
X		EYES		

PRO.	GM TRIM	EMB	R.O.	H.T. GAN
GM/PP/JN	GWT 17	GWT 17		1 Apr 92

SIGNATURE Gary Thurlow DATE 24 Mar 92

COMMENT:

In contrast to the fibrosis of the pulmonary trunk previously observed, it is a circumferential subendothelial change rather than extending into the tunica media. The cause of the aortic mineralization and the pulmonary pyogranuloma are not known. The pulmonary fibrosis coded above was in the same section of lung as the granuloma and is likely a related lesion.

GARY B. MARIT, MAJ, VC, USA
Army Medical Research Unit
Toxicology Division

3 April 1992

PATHOLOGY CLINICAL RECORD						ACCESSION NO. 453-92
T.D.NO. 005	ANIMAL NO. 13-7	DATE DIED NA	DEPT. THV	SEX M	DISP. A	CONDITION G

SPECIES	STRAIN	SOURCE NEC. NO.	ORIGIN	INVESTGATOR
PIG	NA	NA	AF	COOPER

AGENT	CONCENTRATION	EUTHANASIA	NEC. DATE	TIME DIED
NA	NA	PENTABARB	18MAR92	NA

GENERAL CONDITION
GOOD, FAIR, POOR, THIN, EMAC., OTHER,

GROSS EXAMINATION

This pig is in excellent physical and nutritional condition. The only observed lesions are multifocal minimal subendocardial hemorrhage and multifocal minimal epicardial hemorrhage; each lesion is believed to be attributed to perfusion. In addition, this animal had a surgical sight similar to the other treated pigs. Animal weights and organ weights and measurements are on a separate attached sheet. Organ weights were rounded to the nearest tenth of a gram.

HISTOPATHOLOGIC EXAMINATION

1. Proximal pulmonary trunk: Fibrosis, multifocal, segmental, minimal.

2. Heart, right ventricle: Hemorrhage and edema, focally extensive, moderate.

3. Heart, left ventricle: Fibrosis, focal, minimal.

4. Lung: Lymphoid aggregates, multifocal, minimal to mild.

X FOR TISSUE TAKEN		X FOR EXAM MICRO.
	NASAL SECTION	
	BONE	
	BONE MARROW	
	TRACHEA	
	LARYNX	
	ESOPHAGUS	
	THYROID	
	PARATHYROIDS	
X	LUNGS	
X	HEART	
X	LIVER	
X	GALLBLADDER	
X	SPLEEN	
	THYMUS	
	MAND. LYMPH ND.	
	MEST. LYMPH ND.	
X	KIDNEYS	
X	ADRENALS	
	SALIVARY GLAND	
	URIN. BLADDER	
	STOMACH	
	DUODENUM	
	PANCREAS	
	JEJUNUM	
	ILEUM	
	COLON	
	ANUS	
	TESTES/OVARIES	
	SEM.VES./UTERUS	
	PROSTATE/VAGINA	
	SKIN	
	MUSCLE	
	NERVE	
	MAMMARY GLAND	
	PITUITARY	
X	BRAIN	
X	EYES	

PRO.	TRIM	EMB	R.O.	H.T.
GM/PP/JN	GM JWN 17	JWN 17		GAN 1 Apr 92

SIGNATURE Jerry Nicholson DATE 24 Mar 92

COMMENT:

The pulmonary artery fibrosis is similar to but less severe than that seen in animal 452-92. The hemorrhage and edema observed in the heart corresponds to one of the grossly observed lesions and is likely attributed to perfusion.

Gary B. Marit

GARY B. MARIT, MAJ, VC, USA
Army Medical Research Unit
Toxicology Division

3 April 1992

AN INQUIRY INTO THE CHRONIC EFFECTS OF POSITIVE PRESSURE BREATHING

NARRATIVE PATHOLOGY REPORT

GROSS OBSERVATIONS:

At necropsy all pigs utilized in this study were in good general condition. Subendocardial hemorrhage was observed in the control and two test animals; one test pig also had subepicardial hemorrhage. One animal had a small nodule in the lung. Animal and organ weights, organ measurements, and complete gross observations are included in the individual animal's Pathology Clinical Record. Statistical analysis revealed a significant difference in the increased weight of the left atrium in the test pigs versus the control. The statistical worksheet is attached.

HISTOPATHOLOGY:

The histopathologic diagnosis for each tissue alteration and comment is included in the individual animal's Pathology Clinical Record and an Addendum Narrative Report. Analysis of the findings failed to disclose any significant differences between the control and test pigs. The hemorrhages in the heart are attributed to perfusion. The pulmonary nodule observed in pig 452-92 is a pyogranuloma and is most likely in response to aspirated foreign material.

DISCUSSION:

Gross and histologic examination of the left atrial myocardium and gross examination of the mitral valve failed to explain the increased left atrial weight in the test pigs. Because of the small number of pigs utilized in this study it is possible that the variation in the atrial weights may be within the normal range. If the difference is real a functional deficit in the mitral valve is a possible explanation. Perhaps the echocardiographic data collected could resolve this question.

GARY B. MARIT, MAJ, VC, USA
Army Medical Research Unit
Toxicology Division

30 April 1992

ADDENDUM PATHOLOGY REPORT (#s 448-92 and 450-92 to 453-92)

Histopathologic examination of additional sections of the pulmonary trunk (and aorta) from the control pig (448-92) revealed circumferential and multifocal dense fibrosis similar to the other pigs on the study. These areas of fibrosis occurred at or near the pulmonic valve and are believed to be a normal morphologic finding.

Most of the additional sections of aorta and pulmonary arteries from the test pigs (450-92 to 453-92) were essentially normal. There was usually one section that demonstrated fibrosis similar to that seen in the original sections; however, each was believed to have been taken from essentially the same area (near the pulmonic valve). The mineralization of the distal aorta observed in pig 452-92 was not seen in subsequent recut sections.

Gary B Marit

GARY B. MARIT, MAJ, VC, USA
Army Medical Research Unit
Toxicology Division

30 April 1992